PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference LEA36871-WO	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/EP2004/009202	International filing date *(day/month/year)* 17 August 2004 (17.08.2004)	Priority date *(day/month/year)* 30 August 2003 (30.08.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant BAYER HEALTHCARE AG		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☐	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 28 February 2006 (28.02.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	Authorized officer Ellen Moyse Telephone No. +41 22 338 89 75

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

RECD 21 FEB 2005
WIPO PCT

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/009202	17.08.2004	30.08.2003

International Patent Classification (IPC) or both national classification and IPC
C12Q1/37

Applicant
BAYER HEALTHCARE AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☐ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/009202

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-26[completely]

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☒ the claims, or said claims Nos. 1-25[partially] are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 1-25[partially], 26[completely]

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-25[partially]

Reference is made to the following documents:

D1: WO03033731.

Re Item III

Present claims 1-25 [partially] relate to an extremely large number of possible diseases. In fact, the term "hematological disorders" used to identify the different diseases is so broad and vague that a lack of clarity within the meaning of Art. 6 PCT arises. Serious doubts are present with regard to the technical validity of the present invention in as far as hematological diseases are concerned it is clear from the data of Table 1, page 102, there is no data to substantiate a correlation between hematological disorders and KLK9 expression at all. Therefore, in as far as hematological diseases are concerned the present application is considered to provide no disclosure for a correlation of KLK9 with hematological diseases. The subject-matter of claims 1-25 [partially] therefore does not fulfill the requirements of Articles 5 PCT (disclosure) and 6 PCT (support) in as far as hematological diseases are concerned.
The lack of support and disclosure of claim 1-25 [partially] is such that a meaningful opinion as to novelty, inventive step and industrial applicability cannot be given with regard to the subject-matter of claim 1-25. Consequently, an opinion as to novelty, inventive step and industrial applicability of the subject-matter of claims 1-25 [partially] will not be given.

Present claims 19-21, 24 and 25 relate to pharmaceutical compositions, their production and their use defined by reference to a desirable characteristic or property, namely binding to or regulating the activity of a KLK9 polypeptide. The claims cover all pharmaceutical compositions having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such pharmaceutical compositions. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope was impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the pharmaceutical compositions by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Therefore, the search has been carried out for those parts of the claims which appear

to be clear, namely those parts relating to the examples (anti sense oligonucleotide, antibody).

Re Item IV

According to the description the problem to be solved in the present application relates to novel disease associations of KLK9 (page 6, last paragraph). The single general concept which can be identified as a priori linking the various claimed inventions is the notion that KLK9 is (potentially) associated with diseases.

WO03033731 (claim 1) discloses the association between KLK9 and ovarian cancer. In the light of this document, the above identified single general concept is not new and can thus not be the single general inventive concept as required by Rule 13.1 PCT. The present application is therefore considered not to fulfil the requirement of unity as laid down in Rule 13.1 PCT. The objective problem is then to provide further disease associations for KLK9. Each of the different disease-associations found is then a separate solution to this problem not sharing a special technical feature in the sense of Rule 13.2 PCT.

Consequently, the groups of inventions are split up as follows: diagnostics, therapeutics and methods of screening for therapeutics, relating to diseases associated with KLK9, in which the diseases are: 1) hematological diseases, 2) cardiovascular diseases, 3) neurological disorders, 4) metabolic disorders, 5) urological diseases, 6) cancer, 7) inflammation diseases, 8) dermatological disorders and 9) gastroenterological diseases,

No other technical features could be identified that form a technical relationship among each of the separate inventions claimed and which could be considered as a special technical feature within the meaning of Rule 13.2 PCT.

Therefore, the examination of claims 1-25 [partially] has only been carried out in as far as they concern invention 1.